In re Application of: Peter ASSAF et al

Serial No.: 10/555,664 Filed: November 4, 2005

Office Action Mailing Date: October 7, 2008

Examiner: Sun Jae Y. Loewe Group Art Unit: 1626 Attorney Docket: 30724

In the claims:

Please amend the claims as follows:

- 1-5. (Canceled)
- 6. (Currently amended) An NO-donating compound having the general formula I:

$$X-A$$
 S_1
 S_1
 S_1
 S_2
 S_3
 S_4
 S_4

Formula I

wherein:

A is selected from the group consisting of alkyl, amine, aryl, C-amide, carbonyl, hydrazine, N-amide and any combination thereof, or absent;

X is a heteroaryl selected from the group consisting of benzodioxole, benzothiophene, diazole, dithiolane, furan, imidazole, indole, phthalazine, piperidine, pyrazine, pyrazole, pyridine, pyridinyl, pyrimidine, pyrrolidine, quinoline, thiadiazole, thiazole and thiophene;

B is an ethylene chain;

Y is -ONO₂; and

Z is methyl,

the compound being such that when NO is released from the compound a residue which is a naturally occurring metabolite is formed, thereby decreasing a development of tolerance to the NO donating compound upon repetitive administration thereof.

7-16. (Canceled)

17. (Previously presented) The NO-donating compound of claim 6, wherein said heteroaryl is pyridine.

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18-31. (Canceled)

32. (Previously presented) The NO-donating compound of claim 6, being selected from the group consisting of:

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3-[4-Methyl-5-(2-nitrooxy-ethyl)-thiazole-2-yl]-pyridine (Pet-12);
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2-Chloro-3-[4-methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-6-trifluoromethyl-pyridine (**Pet-18**);

Diethyl-{3-[4-methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-pyridin-4-yl}-amine (Pet-19);

2-Methyl-5-[4-methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-pyridine (Pet-20);

3-[4-Methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-pyridine 1-oxide (Pet-21);

5-[4-Methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-2-trifluoromethyl-pyridine (Pet-22);

2-Methoxy-6-[4-methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-pyrazine (**Pet-23**); Methyl-{6-[4-methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-pyrazin-2-yl}-amine

(Pet-24);

2-Ethyl-4-[4-methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-pyridine 1-oxide (**Pet-25**);

5-[4-Methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-2-trifluoromethyl-pyridine 1-oxide (**Pet-26**);

3-(4-Amino-2-methyl-pyrimidin-5-ylmethyl)-4-methyl-5-(2-nitrooxy-ethyl)-thiazol-3-ium; chloride (Pet-68);

2-Furan-2-yl-4-methyl-5-(2-nitrooxy-ethyl)-thiazole (Pet-69);

4-Methyl-5-(2-nitrooxy-ethyl)-2-thiophen-2-yl-thiazole (**Pet-71**);

2-Benzo[b]thiophen-2-yl-4-methyl-5-(2-nitrooxy-ethyl)-thiazole (Pet-72);

[4-Methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-pyridin-3-ylmethyl-amine (**Pe-80**);

4-[4-Methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-pyridine (Pet-81);

2-(3,5-Dimethyl-pyrazol-1-yl)-4-methyl-5-(2-nitrooxy-ethyl)-thiazole (Pet-

83);

5-[4-Methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-1H-imidazol-4-ylamine (Pet-

84);

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- 4-Methyl-5-(2-nitrooxy-ethyl)-2-thiophen-2-ylmethyl-thiazole (Pet-86);
- 4-Methyl-5-(2-nitrooxy-ethyl)-2-(1-thiophen-2-yl-ethyl)-thiazole (Pet-87);
- [4-Methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-thiophen-2-yl-methanone (Pet-88);
- 4-Methyl-5-(2-nitrooxy-ethyl)-2-(nitrooxy-thiophen-2-yl-methyl)-thiazole (**Pet-95**);
 - 2-[4-Methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-pyrazine (Pet-125);
 - 2-[4-Methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-pyrazine 4-oxide (Pet-126);
- 2-[4-Methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-pyrazine 1,4-dioxide (Pet-127);
 - 2-Ethyl-5-[4-methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-pyridine (Pet-144);
- 4-Methyl-5-(2-nitrooxy-ethyl)-thiazole-2-carboxylic acid N'-phthalazin-1-yl-hydrazide (Pet-153);
 - N-[4-methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-nicotinamide (Pet-154);
 - N-[4-methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-1-oxy-nicotinamide (Pet-156);
- 4-Methyl-5-(2-nitrooxy-ethyl)-thiazole-2-carboxylic acid pyridin-3-ylamide (Pet-170);
 - 3-[4-Methyl-5-(2-nitrooxy-ethyl)thiazol-2-ylmethyl]-1H-indole (Pet-172);
 - [4-Methyl-5-(2-nitrooxy-ethyl)-2-yl]-pyridin-4-yl-amine (Pet-174); and
- 4-{4-[4-Methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-phenyl}-[1,2,3]thiadiazole (**Pet-178**).
- 33. (Previously presented) A pharmaceutical composition comprising, as an active ingredient, the NO-donating compound of claim 6 and a pharmaceutically acceptable carrier.
 - 34-64. (Canceled)
- 65. (Previously presented) A medical device comprising the NO-donating compound of claim 6 and a delivery system configured for delivering said NO-donating compound to a bodily site of a subject.

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66. (Original) The medical device of claim 65, wherein said NO-donating compound forms a part of a pharmaceutical composition, said pharmaceutical composition further comprising a pharmaceutically acceptable carrier.

- 67. (Original) The medical device of claim 65, wherein said delivering is effected by inhalation.
- 68. (Original) The medical device of claim 67, wherein said delivery system is selected from the group consisting of a metered dose inhaler, a respirator, a nebulizer inhaler, a dry powder inhaler, an electric warmer, a vaporizer, an atomizer and an aerosol generator.
- 69. (Original) The medical device of claim 65, wherein said delivering is effected transdermally.
- 70. (Original) The medical device of claim 69, wherein said delivery system is selected from the group consisting of an adhesive plaster and a skin patch.
- 71. (Original) The medical device of claim 65, wherein said delivering is effected topically.
- 72. (Original) The medical device of claim 71, wherein said delivery system is selected from the group consisting of an adhesive strip, a bandage, an adhesive plaster, a wound dressing and a skin patch.
- 73. (Original) The medical device of claim 65, wherein said delivering is effected by implanting the medical device in a bodily organ.
- 74. (Original) The medical device of claim 73, wherein said delivery system is selected from the group consisting of an aortic aneurysm graft device, an atrioventricular shunt, a catheter, a defibrilator, a heart valve, a hemodialysis catheter, a hemodialysis graft, an indwelling arterial catheter, an indwelling venous catheter, a

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needle, a pacemaker, a pacemaker lead, a patent foramen ovale septal closure device, a stent, a stent graft, a suture, a synthetic vascular graft, a thread, a tube, a vascular anastomosis clip, a vascular aneurysm occluder, a vascular clip, a vascular prosthetic filter, a vascular sheath and a drug delivery port, a venous valve and a wire.

75. (Original) The medical device of claim 73, wherein said organ is selected from the group consisting of a pulmonary cavity, a blood vessel, an artery, a vein, a capillary, a heart, a heart cavity and a visceral organ.